Cancer Risk and Residential Proximity to Cranberry Cultivation in Massachusetts

ABSTRACT

Objectives. This study evaluated the relationship between cancer risk and residential proximity to cranberry cultivation.

Methods. A population-based case–control study was conducted. Cases, diagnosed during 1983 through 1986 among residents of the Upper Cape Cod area of Massachusetts, involved incident cancers of the lung (n = 252), breast (n = 265), colon–rectum (n = 326), bladder (n = 63), kidney (n = 35), pancreas (n = 37), and brain (n = 37), along with leukemia (n = 35). Control subjects were randomly selected from among telephone subscribers (n = 184), Medicare beneficiaries (n = 464), and deceased individuals (n = 723).

Results. No meaningful increases in risk were seen for any of the cancer sites except for the brain. When latency was considered, subjects who had ever lived within 2600 ft (780 m) of a cranberry bog had a twofold increased risk of brain cancer overall (95% confidence interval [CI] = 0.8, 4.9) and a 6.7-fold increased risk of astrocytoma (95% CI = 1.6, 27.8).

Conclusions. Residential proximity to cranberry bog cultivation was not associated with seven of the eight cancers investigated; however, an association was observed with brain cancer, particularly astrocytoma. Larger, more detailed studies are necessary to elucidate this relationship. (*Am J Public Health.* 1996;86: 1289–1296)

Ann Aschengrau, ScD, David Ozonoff, MD, MPH, Patricia Coogan, MPH, Richard Vezina, MPH, Timothy Heeren, PhD, and Yuqing Zhang, ScD, MB

Introduction

Since the inception of the Massachusetts Cancer Registry in 1982, statistically significant increases in the standardized incidence ratios for cancers of the lung, breast, colon–rectum, and blood-forming organs and statistically unstable excesses of cancers of the kidney, bladder, and pancreas have been observed in the Upper Cape Cod area relative to statewide averages.[1] The elevated rates cannot explained by differences in age, gender, or reporting practices.[1]

During this period, many environmental hazards affecting the Upper Cape area also have come to public attention, including groundwater and air contamination from a variety of sources such as the Massachusetts Military Reservation (currently a Superfund National Priority List site), perchloroethylene in water distribution system pipes,[2] and possible exposure to herbicides and pesticides among residents who live near cranberry cultivation.

Residential proximity to cranberry bog cultivation has warranted concern because, unlike most of Massachusetts, the Upper Cape region has had substantial acreage devoted to cranberry cultivation since the late 1800s.[3–5] Numerous herbicides, insecticides, and fungicides have been approved for use on the bogs for varying periods of time since the 1930s. These chemicals include kerosene, dichlorobenil, DDT, dieldrin, aldrin, 2,4,5-trichlorophenoxyacetic acid, heptachlor, chlordane, pyrethrum, malathion, parathion, cryolite, lead arsenate, carbaryl, diazinon, azinphos-methyl, and aminotriazole (I. Demoranville, Director, Cranberry Experiment Station, East Wareham, Mass, personal communication, March 1989).[4–7]

From the 1930s through the mid-1950s, these chemicals were applied primarily through ground-based methods, including truck and power nozzle spraying, power dusting, and hand spraying (I. Demoranville, personal communication, March 1989).[5] From the mid 1950s through the 1970s, aerial methods were used more often (both fixed-wing aircraft and helicopters). In the 1980s, chemicals were applied primarily through sprinkler systems in the bogs.

We undertook a population-based case–control study to evaluate the relationship between nine types of cancer (lung, breast, colorectal, bladder, kidney, pancreas, brain, and liver cancer, along with leukemia) and several sources of environmental contamination in the region.[2,8,9] The current report focuses on the risk of cancer among Upper Cape residents who lived near cranberry cultivation. On the basis of studies of occupational and nonoccupational exposure to agricultural chemicals similar to those applied to the bogs,[10–19] we hypothesized that positive associations were likely for cancers of the kidney, colon–rectum, brain, and hematopoietic system.

Ann Aschengrau, Richard Vezina, Timothy Heeren, and Yuqing Zhang are with the Department of Epidemiology and Biostatistics, and David Ozonoff and Patricia Coogan are with the Department of Environmental Health, Boston University School of Public Health.

Requests for reprints should be sent to Ann Aschengrau, ScD, Boston University School of Public Health, 80 E Concord St, B303a, Boston, MA 02118.

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Note. The views expressed here are the authors' and do not necessarily represent those of the Massachusetts Department of Environmental Protection or the Massachusetts Department of Public Health.

TABLE 1—Selection and Enrollment of Cancer Case Patients and Control Subjects, Upper Cape Cod, Mass, 1983 through 1986

	Selected, No.	Excluded, No.			Interviewed, No.
		Never Found or Contacted	Not Eligible	Physician or Subject Refusal	
Case subjects, by cancer site					
Lung	326	46	8	20	252
Breast	334	33	6	30	265
Colorectal	420	51	3	40	326
Bladder	79	7	0	9	63
Kidney	42	6	0	1	35
Pancreas	43	3	1	2	37
Brain	42	1	1	3	37
Leukemia	44	4	2	3	35
Control subjects, by selection method					
Health Care Financing Administration	611	21	53	73	464
Deceased	918	97	27	71	723
Random-digit dialing	2236	456	1531[a]	65	184

[a]Includes 129 individuals who refused to answer the eligibility screening questions.

Methods

Selection and Enrollment of Study Population

The cases involved incident cancers of the lung (n = 326), breast (n = 334), colon–rectum (n = 420), bladder (n = 79), kidney (n = 42), pancreas (n = 43), brain (n = 42), and liver (n = 6), as well as leukemia (n = 44), diagnosed from 1983 through 1986 among permanent residents of the five Upper Cape towns (Barnstable, Bourne, Falmouth, Mashpee, and Sandwich) and reported to the Massachusetts Cancer Registry. Liver cancer is omitted from this report since there were too few cases for meaningful evaluation.

Cancer incidence rates from the Massachusetts registry are comparable to those of the nearby Connecticut registry and the American Cancer Society, indicating good ascertainment for the cancers and geographic area under study.[20] The rates for all sites except brain and liver were elevated at the start of the study among men and/or women in at least one of the Upper Cape towns. Brain and liver cancer were not initially included for study but were added during the first year because of their possible environmental etiology.[21]

The control subjects came from the same population that gave rise to the cases: permanent residents of the Upper Cape towns during 1983 through 1986. Since many case patients were elderly or deceased at the time the study began, three sources were used to identify comparable controls efficiently.

A random sample of living control subjects less than 65 years of age who resided in the Upper Cape towns during the case ascertainment period was selected via random-digit dialing. According to the 1980 census, more than 95% of Massachusetts housing units had telephone service.[22] A total of 2236 residential households were identified (Table 1). Of these, 249 households with an eligible respondent were identified, and 184 of these respondents were interviewed (74%).

Living control subjects 65 years of age and older were identified through lists of the elderly provided by the Health Care Financing Administration (HCFA). These lists are estimated to include 95% of individuals 65 years of age and older in the United States.[23] Six hundred eleven HCFA control subjects were randomly selected from the Upper Cape population by means of an age- and gender-stratified sampling scheme. Vital status and residence were determined, and all deceased individuals and non–Upper Cape residents were excluded.

Control subjects who had died from 1983 through 1989 were randomly selected from a listing of all Upper Cape resident deaths, furnished by the Massachusetts Department of Vital Statistics and Research, that included all individuals regardless of cause of death. A sampling scheme stratified on age, gender, and year of death produced 918 deceased control subjects. The deceased control subjects' residences during the case ascertainment period were determined, and nonresidents were excluded.

Follow-Up and Interviews

Current addresses and telephone numbers of subjects or their next of kin were determined through Massachusetts Cancer Registry, HCFA, and physician records; voter registration lists; driver's license and vital statistics records; and telephone directories. Permission to interview the living case patients was obtained from physicians, in accordance with Massachusetts Cancer Registry guidelines.

Structured interviews were carried out by trained personnel to obtain information on demographic characteristics, smoking, alcohol consumption, medical conditions, reproductive events, occupations since the age of 18 years, and a residential history from 1943 through 1986. These calendar years were defined as the study period since they encompassed the relevant etiologic period for the inception and development of the cancers under study.

Seventy-nine percent of the case patients, 74% of identified eligible random-digit dial control subjects, 76% of the HCFA control subjects, and 79% of next of kin for deceased control subjects were interviewed (Table 1). Response rates were fairly similar across cancer sites (77% to 88%; see Table 1). Eighty-six percent of the interviews were conducted by telephone; the remainder were conducted in person. Interviews were conducted with next of kin or household members when subjects were very ill or deceased.

Interviewed and noninterviewed case and control subjects were similar demographically. Of the noninterviewed case patients, 39.0% were male, 96.5% were White, 80.3% were 60 years of age and older, and 44.0% were alive at the time of the interview. By comparison, 41.2% of the noninterviewed HCFA and deceased control subjects were male, 94.7% were White, and 89.5% were 60 years of age and older; 43.5% were alive at the time of the interview. No data were available on noninterviewed random-digit dialing control subjects.

Pathologic records of the cancer cases confirmed that they were nonmetastatic in origin. Among the brain cancer cases, there were astrocytomas (n = 9),

TABLE 2—Distribution (%) of Selected Characteristics of Cancer Case Patients and Control Subjects

Characteristic	Lung Cancer		Breast Cancer		Colorectal Cancer		Bladder Cancer		Kidney Cancer		Pancreas Cancer		Brain Cancer		Leukemia	
	Case Patients (n = 243)	Control Subjects (n = 1206)	Case Patients (n = 258)	Control Subjects (n = 686)	Case Patients (n = 311)	Control Subjects (n = 1158)	Case Patients (n = 61)	Control Subjects (n = 853)	Case Patients (n = 35)	Control Subjects (n = 778)	Case Patients (n = 36)	Control Subjects (n = 622)	Case Patients (n = 36)	Control Subjects (n = 703)	Case Patients (n = 34)	Control Subjects (n = 738)
Female	42.0	57.1	100.0	100.0	46.3	56.2	26.2	47.3	34.3	51.7	63.9	61.4	47.2	57.6	52.9	52.9
White	96.3	96.6	98.4	96.8	96.1	96.3	98.4	96.6	94.3	96.9	97.2	96.9	100.0	96.6	97.1	96.2
Age, y[a]																
1–49	3.7	5.4	12.0	7.1	1.9	3.3	0.0	1.4	2.9	1.3	0.0	0.2	22.2	2.1	17.7	4.6
50–59	12.4	10.3	14.7	12.0	9.0	10.3	9.8	10.1	8.6	7.1	5.6	2.4	13.9	10.7	2.9	6.5
60–69	38.3	33.2	30.2	33.8	25.4	34.3	42.6	39.8	28.6	42.5	13.9	33.3	22.2	38.0	20.6	35.6
70–79	35.8	33.7	27.1	27.6	42.4	34.0	36.1	33.9	51.4	39.8	58.3	45.5	30.6	35.3	32.4	37.3
80+	9.9	17.4	15.9	19.6	21.2	18.4	11.5	14.8	8.6	9.4	22.2	18.7	11.1	13.9	26.5	16.0
Educated at least 12 years	81.3	80.9	83.1	82.7	79.1	80.3	68.4	81.5	79.4	83.2	85.7	80.7	82.9	82.4	69.7	80.1
Alive at interview	17.7	46.8	67.4	55.1	54.7	46.9	65.6	57.0	51.4	61.5	5.6	36.2	22.2	37.7	23.5	34.6
Ever regular cigarette smoker	93.4	65.8	59.0	53.9	60.7	63.9	88.5	66.5	74.3	66.7	50.0	65.3	63.9	68.4	64.7	68.5
Ever regular alcohol drinker	93.8	84.0	81.3	77.6	82.4	83.0	80.0	86.5	94.1	85.5	68.6	81.9	88.9	83.2	85.3	83.9
Ever had occupational exposure to pesticides and herbicides[b]	14.5	8.3	3.3	4.5	6.9	8.6	10.2	8.5	8.8	7.1	9.7	6.8	6.5	6.5	10.0	9.3
Ever gardened with pesticides or herbicides	41.4	38.5	31.4	32.4	38.2	38.5	41.4	39.2	35.3	38.6	32.3	37.9	46.9	36.9	55.9	40.0
Any residence ever treated for termites	23.5	21.9	26.3	22.3	16.2	21.3	12.1	21.4	24.2	21.0	18.8	19.2	21.9	23.1	32.3	20.0

[a]At diagnosis or index year.
[b]Based on answers to direct questions regarding occupational exposure to pesticides, herbicides, and cranberry work and industry and job title information.

TABLE 3—Presumed Calendar Years of Cranberry Bog Operation

Calendar Years That Bog Was Seen in Aerial Photographs	Presumed Years of Operation during the Study Period
1951 alone	1943–1961
1971 alone	1961–1977
1984 alone	1977–1986
1971, 1984	1966–1986
1951, 1971	1943–1977
1951, 1984	1943–1961, 1977–1986
1951, 1971, 1984	1943–1986

Note. The study period encompassed 1943 through 1986.

glioblastomas (n = 15), other gliomas (n = 4), and other and unspecified subtypes (n = 8).

Site-specific control groups were chosen by stratifying each case group on the basis of age, gender, vital status, and, if deceased, year of death and then choosing all control subjects who fell into a stratum with at least one case. An index year was then selected for each control group to correspond to the diagnosis date for the cases. The median diagnosis year of the case group was selected as the index year for its control group, and only exposures that occurred before the index year were counted. Control subjects who moved to the Upper Cape after the index year, and case and control subjects with incomplete residential histories, were excluded (0.0% to 4.0% of case patients and 6.0% to 10.1% of control subjects). The number of case and control subjects included in the analysis is provided in Table 2.

Exposure Assessment

All subjects' residences in the five Upper Cape towns during the study period were located on United States Geological Survey maps; detailed residential tax assessment maps were also used in this procedure. All mapping was conducted without knowledge of a subject's disease status.

Bog locations and acreage were obtained from aerial land use photographs and maps prepared by the Department of Forestry and Wildlife Management at the University of Massachusetts. Maps were available for 3 years: 1951, 1971, and 1984. Outlines of cranberry bogs at each year were transferred to a set of acetate overlays. No information was available on when a bog went into or out of production between these reference points, so certain assumptions were made about the calendar years during which the bogs operated (see Table 3).

Distance, direction, and acreage were used to describe potential exposure. The exposure zone was defined as the 2600-ft (0.5-mile [780 m]) area around a bog on the basis of results from a pesticide drift study indicating that the most "driftable" portion of a pesticide formulation (droplets less than 100 microns in diameter) could be carried to a distance of a half mile from the flight line.[24] The distance of all subject residences within 2600 ft was measured to the nearest 100 ft from the bog's nearest edge. All exposure assessments were conducted without knowledge of who was a case or a control subject. No information was available on the types of herbicides and pesticides or application methods used on specific bogs.

Data Analysis

The analysis examined proximity to cranberry bog cultivation in relation to each cancer site. Exposure was examined as a dichotomous variable (i.e., ever vs never exposed) and was also specified according to distance, duration, and direction. The referent category consisted of subjects who had always lived more than 2600 ft from a bog. Analyses were conducted with and without taking the latent period for cancer into account. The latent periods used were 5 years for leukemia and 15 years for the other cancer sites.[25–27]

Exposure odds ratio (ORs) were used to estimate the strength of the relationship (relative risk) between proximity to cranberry bog cultivation and cancer site. Following the World Health Organization oncology classification scheme,[28] odds ratios were also calculated for the following brain cancer subtypes: astrocytoma (n = 9), glioblastoma (n = 15), other gliomas (n = 4), and other and unspecified cases (n = 8). Ninety-five percent confidence intervals (CIs) for the crude odds ratios were computed by means of Miettinen's test-based method (if there were at least five exposed case patients) or Fisher's exact method (if there were fewer than five exposed case patients).[29,30]

Multiple logistic regression models were used to control simultaneously for potential confounding variables.[31] Gender, age at diagnosis or index year, vital status, occupational exposure to herbicides and pesticides (including work in cranberry cultivation), and residential exposure to herbicides and pesticides from gardening and home termite treatment were controlled in all adjusted analyses. In addition, other well-known strong risk factors for each cancer site were controlled if at least three case patients had a positive history of the potential confounder. Usual number of cigarettes smoked; cigar, pipe, and passive smoking; usual alcohol consumption; and history of a cancer-associated job (arsenic, asbestos, chromium, coke oven, coal tar pitch, iron ore, uranium, nickel refinery, and rubber manufacturing workers) were controlled in the lung cancer analysis. Family history of breast cancer, age at first live birth or stillbirth, prior benign breast disease, and prior breast cancer were controlled in the breast cancer analysis. Usual alcohol consumption, family history of polyposis, history of inflammatory bowel disease or ulcerative colitis, and history of a cancer-associated job (asbestos, coke oven, solvent workers) were controlled in the colorectal cancer analysis. Usual number of cigarettes smoked and history of a urinary tract infection or stone were controlled in the kidney cancer analysis. Usual number of cigarettes smoked, history of a urinary tract infection or stone, and history of a cancer-associated job (rubber and cable manufacturing, dye manufacturing, leather workers) were controlled in the bladder cancer analysis. Usual number of cigarettes smoked and usual alcohol consumption were controlled in the pancreatic cancer analysis. Finally, prior medical treatment with irradiation was controlled in the leukemia analysis.[32,33] Maximum likelihood estimates of the standard errors were used in calculating 95% confidence intervals for the adjusted odds ratios.[34]

Results

The case and control subjects were mainly White and elderly, and most had 12 or more years of education (Table 2). The proportion alive at interview varied according to cancer site from 5.6% for pancreas cancer case patients to 67.4% for breast cancer case patients. Prior occupational exposure to pesticides and herbicides, including work in cranberry cultivation, was relatively uncommon among study subjects, while gardening with chemicals and residential termite treatment were more frequent.

Whether or not latency was considered, no meaningful increases were seen

in the crude or adjusted relative risks for any of the cancer sites, except for the brain (Table 4). When the latent period was considered, subjects who had ever lived within 2600 ft of a cranberry bog had a 2.5-fold increase in the crude relative risk of brain cancer (95% CI = 1.2, 5.1) that fell to 2.0 when confounding variables were controlled (95% CI = 0.8, 4.9). These relative risks were not elevated when the latent period was ignored, supporting the idea that the exposure initiated rather than promoted the cancer.

Among the brain cancer subtypes, the relative risks were considerably higher for astrocytomas (adjusted ORs = 6.7 and 2.0, respectively, with and without latency) than for the other cell types (Table 5). A dose–response relationship was seen with distance but not bog acreage or exposure duration among the astrocytoma cases, but these results were highly unstable since there were so few exposed astrocytoma case patients (zero to four) in any given category.

Since brain cancer was also associated with other environmental exposures in the Upper Cape area (including proximity to the military base runways),[8,9] analyses were conducted that examined subjects who were not exposed to any other factor (4 brain cancer case patients [2 with astrocytomas, 1 with glioblastoma, and 1 with an unspecified neoplasm] and 38 control subjects).[35] The crude and adjusted relative risks of brain cancer among these individuals remained elevated (crude OR = 3.8, 95% CI = 0.8, 15.7; adjusted OR = 3.1, 95% CI = 0.2, 42.5).

Regarding other potential sources of pesticide exposure, more brain cancer case than control subjects (46.9% vs 36.9%) reported gardening with pesticides and herbicides; however, fewer case than control subjects (21.9% vs 23.1%) reported ever living in a residence that was treated for termites, and an identical proportion of brain cancer case patients and control subjects (6.5%) reported occupational exposure to pesticides and herbicides (Table 2).

TABLE 4—Number of and Odds Ratios for Cancer Case Patients and Control Subjects Who Had Ever Lived within 2600 ft of a Cranberry Bog, with and without Latency

	No. Exposed Case Patients	No. Exposed Control Subjects	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)
With latency				
Lung cancer	46	195	1.2 (0.9, 1.7)	1.1 (0.7, 1.7)
Breast cancer	47	106	1.2 (0.8, 1.8)	1.3 (0.9, 2.0)
Colorectal cancer	44	191	0.8 (0.6, 1.2)	0.9 (0.6, 1.4)
Bladder cancer	6	140	0.6 (0.6, 1.3)	0.5 (0.2, 1.3)
Kidney cancer	4	122	0.7 (0.2, 2.0)	0.7 (0.2, 2.3)
Pancreas cancer	4	98	0.7 (0.2, 2.0)	0.4 (0.1, 1.8)
Brain cancer	11	106	2.5 (1.2, 5.1)	2.0 (0.8, 4.9)
Leukemia	10	195	1.2 (0.6, 2.5)	1.1 (0.5, 2.6)
Without latency				
Lung cancer	96	400	1.3 (1.0, 1.8)	1.2 (0.8, 1.7)
Breast cancer	90	213	1.2 (0.9, 1.6)	1.2 (0.8, 1.6)
Colorectal cancer	105	386	1.0 (0.8, 1.3)	1.0 (0.8, 1.4)
Bladder cancer	18	288	0.8 (0.5, 1.5)	0.7 (0.4, 1.3)
Kidney cancer	8	256	0.6 (0.3, 1.3)	0.7 (0.3, 1.6)
Pancreas cancer	13	195	1.2 (0.6, 2.5)	1.0 (0.4, 2.6)
Brain cancer	13	231	1.2 (0.6, 2.3)	0.8 (0.3, 1.8)
Leukemia	12	241	1.1 (0.6, 2.3)	1.0 (0.5, 2.3)

TABLE 5—Number of and Odds Ratios for Exposed Brain Cancer Case Patients, with and without Latency

Cell Type	No. Exposed Case Patients	Crude Odds Ratio[a] (95% Confidence Interval)	Adjusted Odds Ratio[b] (95% Confidence Interval)
With latency			
Astrocytoma (n = 9)	5	7.0 (2.2, 22.3)	6.7 (1.6, 27.8)
Glioblastoma (n = 15)	3	1.4 (0.3, 5.3)	1.4 (0.4, 5.2)
Other gliomas (n = 4)	1	1.9 (0.0, 23.6)	. . .[c] . . .
Other and unspecified (n = 8)	2	1.9 (0.2, 10.7)	1.5 (0.3, 8.5)
Without latency			
Astrocytoma (n = 9)	5	2.6 (0.7, 9.2)	2.0 (0.5, 8.0)
Glioblastoma (n = 15)	4	0.7 (0.2, 2.6)	0.8 (0.2, 2.5)
Other gliomas (n = 4)	1	0.7 (0.0, 8.5)	. . .[c] . . .
Other and unspecified (n = 8)	3	1.2 (0.2, 6.4)	1.2 (0.3, 5.8)

[a]Relative to 106 exposed control subjects with latency and 231 exposed without latency.
[b]See text for variables that were controlled.
[c]There were too few exposed case patients to perform the adjusted analysis.

Discussion

This study found no evidence for increased risks of lung, breast, colorectal, bladder, kidney, and pancreas cancer, and no evidence for an increased risk of leukemia, among individuals who had ever lived with 2600 ft of cranberry cultivation. However, an association was observed for brain cancer, principally astrocytoma. While there was evidence of a dose–response relationship with distance for the astrocytoma case patients, no such relations were seen for bog acreage and exposure duration. Athough these findings are inconsistent, they warrant cautious interpretation since they are based on a small number of exposed case patients.

Several factors tended to decrease the stability of the estimates of association and bias them downward. First, the size of several case groups was small, thus affecting statistical stability. Second, the risk estimates based on all brain cancers combined may have been biased downward since brain cancer cell types have sufficiently different epidemiologic features to suggest different etiologies.[36] Third, residential proximity to cranberry bog cultivation was an imprecise exposure

surrogate. In addition, faulty recall of residential histories, inaccuracies associated with residence mapping, and incorrect assumptions about the years the bogs operated may have further increased exposure misclassification. Since exposure was defined identically for case and control subjects, and assessments were conducted blindly, the misclassification was probably nondifferential and so biased the findings toward the null. Fourth, underascertainment of other sources of pesticide exposure obtained by interview (e.g., occupational exposure to pesticides) was likely since most brain cancer case patients and control subjects were already deceased and their next of kin may have had limited knowledge about these types of exposures. The fact that proxy interviews predominated for both brain cancer case patients and control subjects probably led to nondifferential misclassification, making it difficult to detect associations for these variables.

It is unlikely that these results can be ascribed to observation or selection bias. Even though the interviewers were not blinded, the questionnaire was highly structured, the questions were carefully written and pretested, and the interviewers were experienced. Thus, the possibility of systematic differences in obtaining information was minimized. Recall bias was also unlikely since residential proximity to cranberry bogs was not directly assessed in the interview.

Selection bias was also unlikely since the cancer case patients were selected from all incident cases reported to the state cancer registry. Rates from other sources, including the nearby Connecticut Cancer Registry, indicate nearly complete reporting for the cancer sites and geographic area under study.[20] Furthermore, follow-up and interview rates were high and similar among case patients and control subjects, and the demographic characteristics of interviewed and noninterviewed subjects were similar.

In regard to confounding, age, sex, vital status at interview, occupational and gardening exposure to herbicides and pesticides, residential termite treatment, and other well-known risk factors that occurred with reasonable frequency were included in the multivariate analysis.

However, no information was obtained on reported risk factors for brain cancer such as head trauma[35,37]; diagnostic head x-rays[35,37]; consumption of meat cured with sodium nitrite[37]; paternal occupational exposure to paint, hydrocarbons, metals, petroleum, solvents, and electric fields[38]; in utero or early childhood exposure to barbiturates[39]; higher birthweight[40]; exposure to sick pets[40]; and a family history of neurological disorders.[40] These risk factors have been associated either with brain cancer among children or with intracranial meningiomas among adults (both rare in our population).

No brain cancer case patients in our study had a history of other reported risk factors such as family history of brain cancer[32] or history of radiotherapy to the head,[41] and only one case patient had an occupation (as a chemist) that has been associated with brain cancer in the literature.[32] While residual confounding is a possible explanation for the observed increases in risk, the unmeasured risk factors would have to be very strong confounders to account for the large odds ratio observed for astrocytoma.

There are also several reasons why "multiple testing" is an unlikely explanation for the findings. First, the association was highly specific, that is, limited mainly to one brain cancer cell type. Second, the significance level for astrocytoma association was quite low (adjusted OR = 6.7 with latency, $P = .009$). Third, there is little reason to believe that the different hypotheses examined in this study have any bearing on one another or that a "universal" null hypothesis applies to these data.

Still another reason stems from the numerous published studies that also showed a relationship between brain cancer and occupational and nonoccupational exposure to agricultural chemicals and were the basis of our hypothesis.[10–12,16,42–49] One review of epidemiologic research on cancer among farmers reported that two thirds of the reviewed studies found increased risk ratios for brain cancer.[49] Increases in the risk of brain and/or central nervous system cancer have been observed among farmers and farm managers in Minnesota[42]; agricultural crop production workers in Missouri[43]; non-White farmers in North Carolina[10]; US agricultural extension agents[11]; Canadian agricultural workers[12]; New Zealand orchard, vineyard, tree, and shrub workers[16]; New Zealand farm managers[48]; Swedish agricultural workers[44]; residents of Italian districts with large fruit and wine production[47]; and Italian farmers.[45,46] The increased risk among the Italian farmers was attributed to the use of insecticides, fungicides, herbicides, and fertilizers.[46]

A smaller number of occupational studies have failed to observe an excess risk of brain cancer among farmers.[49–53] These include two investigations among US farmers[49]; a study among farmers, foresters, and fishermen in England and Wales[49]; a death certificate analysis of farm workers in New Jersey, Philadelphia, and Louisiana[50]; a study of gliomas in Swedish farmers, fishermen, and hunters[51]; a study of German agricultural workers[52]; and an ecological analysis of rural farm areas in Quebec with high pesticide use.[53] These null findings may stem from broad exposure definitions and differences in chemical use.

In our population, a small and identical percentage of brain cancer case and control subjects stated that they had ever been employed in cranberry cultivation, agricultural and landscaping activities, or jobs that involved exposure to herbicides and pesticides (6.5% of case patients and control subjects). Controlling for a history of these exposures and other confounders did not materially reduce the magnitude of the association, but data on other sources of pesticides and herbicides may have been underascertained as a result of the high proportion of proxy interviews.

Increases in brain cancer risk have also been observed among individuals with nonoccupational exposure to agricultural activities and chemicals. In a Swedish case–control study of astrocytoma, case patients were more likely than control subjects to have lived in the vicinity of a farm or to have reported exposure to pesticides and herbicides.[54] A case–control study of brain tumors among children in the United States also found that a larger number of case patients than control subjects lived on a farm and were possibly exposed to pesticides from residential insect exterminations.[40]

In summary, we found no evidence of an increased risk of lung, breast, colorectal, bladder, kidney, and pancreas cancer and leukemia among individuals who had ever lived near cranberry cultivation. However, an association was observed for brain cancer, principally astrocytoma. This finding is consistent with results from numerous other published studies of populations with similar occupational and nonoccupational exposures. To our knowledge, this is the first report of cancer risk in relation to nonoccupational exposure to agricultural work. Because our study had numerous limitations, further investigation is warranted. Future studies should

obtain information on the types of herbicides and pesticides and application methods used and should include a large number of cases in order to obtain precise estimates of risk. □

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Preliminary analyses of these data were reported to the Massachusetts Department of Public Health in September 1991.[35] The results reported here differ from those given in that report because of minor corrections in the final study population and adjustment for additional confounding variables. The study questionnaire is available upon request.

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The American College of Preventive Medicine, the Association of Teachers of Preventive Medicine Foundation, the Association of American Medical Colleges, the Association of Preventive Medicine Residents, the journal *Preventive Medicine,* and the Ulrich and Ruth Frank Foundation for International Health announce their annual competition for the best paper in preventive medicine by a medical student. The prize for the best paper is $1000 and it will be published, after editing, in *Preventive Medicine.*

The awardee will be honored at Prevention '97, the annual meeting of the American College of Preventive Medicine and the Association of Teachers of Preventive Medicine, to be held in Atlanta in the spring. All prevention-oriented topics will be considered; papers addressing the implementation of clinical preventive services are encouraged. All submissions must be postmarked by *October 22, 1996.*

For more information, send a self-addressed, stamped envelope to Michelle Kettles, MD, Dept of Preventive Medicine and Environmental Health, University of Kentucky, 1141 Red Mile Rd, Lexington, KY 40504, or to Penny Stern, MD, Dept of Public Health, Cornell University Medical College, 411 E 69th St #301-C, New York, NY 10021.